

## CLAIMS

1. A method for the diagnosis of male infertility, **characterized** by detecting the presence or absence of a mutation or mutations in the *POLG* gene encoding the catalytic subunit of mitochondrial DNA polymerase
- 5 in a biological sample.
2. A method for population-based screening for genetic predisposition to male infertility, **characterized** by detecting the presence or absence of a mutation or mutations in the *POLG* gene encoding the catalytic subunit of mitochondrial DNA polymerase in a biological sample.
- 10 *prosa* 3. A method of claim 1 or 2, **characterized** in that the mutation or mutations are located in the trinucleotide (CAG) microsatellite repeat of the *POLG* gene.
4. A method of claim 3, **characterized** in that the mutation or mutations are located in both alleles of the *POLG* gene in the trinucleotide
- 15 (CAG) microsatellite repeat of the *POLG* gene.
- 20 *prosa* 5. A method of claim 1 or 2, **characterized** in that the mutation or mutations are located in or near a coding region of the *POLG* gene.
6. A method of claim 1 or 2, **characterized** in that one mutation or mutations are located in one allele of the *POLG* gene in the trinucleotide (CAG) microsatellite repeat and another mutation or other mutations in the
- 20 other allele of the mutant *POLG* gene in or near a coding region of the gene.
7. A method of any one of claims 1 to 6, **characterized** in that the detection of the mutation is performed using a gene-technological method.
- 25 8. A method of claim 7, **characterized** in that the detection of the mutation or mutations is performed using the polymerase chain reaction (PCR) or other thermal cycler-based DNA synthetic techniques, molecular cloning in a plasmid or other suitable vector, detection of length variants in a DNA sample by agarose or polyacrylamide gel electrophoresis, gel or capillary
- 30 electrophoresis and analysis of products tagged with a fluorescent or other label incorporated into the DNA, DNA sequence determination and any heteroduplex-based or similar methods for detecting base mismatches or length variants.
- 35 *prosa* 9. A method of any one of claims 1 to 6, **characterized** in that the detection of the mutation or mutations is performed using an immu-

nological method, such as a Western analysis, immunohistology or immunoassay, for characterization of a mutant gene or gene product.

10. A method of claim 9, **characterized** in that the detection of mutation or mutations is performed using immunohistology.

5 11. A use of a mutant form of the *POLG* gene encoding the catalytic subunit of mitochondrial DNA polymerase for the diagnosis or prediction of male infertility.

12. A use of a mutant form of the *POLG* gene encoding the catalytic subunit of mitochondrial DNA polymerase as a diagnostic agent.

10 13. A diagnostic kit, **characterized** in that it comprises reagents capable of identifying the presence or absence of a mutation or mutations in the *POLG* gene encoding the catalytic subunit of mitochondrial DNA polymerase.

15 14. A use of the *POLG* gene as an indicator of other pathological conditions associated with or related to male infertility, including those manifesting in women.

add B2